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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/552,084	12/01/2006	Robert L. Wolfert	DEX0478US.NP	4146

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EXAMINER	
NIEBAUER, RONALD T	
ART UNIT	PAPER NUMBER
1654	

NOTIFICATION DATE	DELIVERY MODE
04/15/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

poreilly@licataandtyrrell.com

Office Action Summary	Application No.	Applicant(s)	
	10/552,084	WOLFERT ET AL.	
	Examiner	Art Unit	
	RONALD T. NIEBAUER	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,16,18-21,24,25 and 30-32* is/are pending in the application.

4a) Of the above claim(s) *3,8,9,16,18-21,24,25 and 30-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-7,10 and 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 October 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/3/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group II (claims 1-11,16,18-21) and the following species:

Variable/s measured: Lp-PLA2 and CRP

Patient disorder/patient population: hypertension

in the reply filed on 1/31/08 is acknowledged. The traversal is on the ground(s) that applicants disagree that Packard (NEJN, 2000) teach claim 1. Applicant argues that the instant application shows that Lp-PLA2 and CRP in combination synergistically predict risk of coronary events better than individually, which is not taught in Packard. Applicants argue that the claims define a special technical feature that defines a contribution over the prior art. With regard to the species election, applicants argue that the search of all species would not be unduly extensive or burdensome. Applicant notes that only nine patient disorders are recited.

This is not found persuasive because as discussed below, Packard teach claim 1 of the instant invention. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., that Lp-PLA2 and CRP in combination synergistically predict risk of coronary events better than individually) are not recited in the instant claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Packard specifically teach a

multivariate assessment on the risk of a coronary event (Table 5). As such, the models used the variables including CRP and Lp-PLA2 (i.e. a combination of risk factors).

Regarding the species election, there would be a search and examination burden because the species require a different field of search (for example, searching different electronic resources or employing different search queries); the prior art applicable to one species would not likely be applicable to another species, the species are likely to raise different non-prior art issues under 35 USC 101 and/or 35 USC 112, first paragraph. Further, there is nothing of record showing the species to be obvious variants.

The requirement is still deemed proper and is therefore made FINAL.

In the instant case the elected species were found in the prior art. As such the examination is limited to the generic claims and claims to the elected species. In the instant case, claim 1 is the only claim that reads on hypertension as claim 18 for example reads on a different subset of patients. In the instant case, claims 3,8 for example read on measuring LDL a non-elected species.

Claims 3,8-9,16,18-21,24-25,30-32 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention/species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 1/31/08.

Claims 12-15,17,22-23,26-29,33-35 have been cancelled.

Claims 1-2,4-7,10-11 are under consideration.

Specification

The disclosure is objected to because of the following informalities:

The use of the trademarks (such as ALEXA FLUOR® 350 and others last paragraph of page 3) has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Appropriate correction is required.

Claim Objections

Claim 10 is objected to because of the following informalities:

Claim 10 recites 'using the ATP III guidelines'. However the meaning of the abbreviation ATP is not set forth in the claim. ATP can mean adenosine triphosphate or alanine-threonine-proline. Page 4 line 22-23 states that ATP refers to Adult Treatment Panel which is taken as the intended meaning of the abbreviation.

Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2,4-7,11 are rejected under 35 U.S.C. 102(b) as being anticipated by Packard et al. (NEJM Oct 19 2000 v343 pages 1148-1155).

Packard teach that there are reports that C-reactive protein (CRP) levels are elevated in those at risk for coronary disease (page 1148 column 2 1st paragraph). Packard teach that lipoprotein-associated phospholipase A2 (Lp-PLA2, also known as platelet-activating factor acetylhydrolase) is a potential predictor of the risk of coronary heart disease (page 1148 column 2 2nd paragraph). Packard confirms that CRP and Lp-PLA2 are indicators of risk of coronary heart disease (page 1152 'discussion' section 1st paragraph). Thus the specific disease recited in claim 2 of the instant invention is met. Packard teach that the patient population includes patients with hypertension (table 1) thus meeting the limitation of the elected patient population. Packard teach that CRP and Lp-PLA2 were measured in aliquots of plasma collected from patients (page 1149 'measurements' section 2nd paragraph) thus the sampling (which is a step of the measuring process) was done simultaneously thus meeting the limitations of claim 4 of the instant invention. Packard also teach that separate enzyme-linked immunoassays were performed for CRP and Lp-PLA2 (page 1149 'measurements' section 2nd and 3rd paragraphs) thus the assaying (which is a step of the measuring process) was performed sequentially thus meeting the limitations of claim 5 of the instant invention. Packard teach that Lp-PLA2 mass was measured (page 1149 'measurements' section 3rd paragraph) thus meeting the limitation of claim 11 of the instant invention. Packard teach that quintile ranges (i.e. divided into 5 classes) were established for the variables (page 1140 'statistical analysis' section 1st paragraph). Since there are 5 classes

there are necessarily high and low levels as well as high, medium, and low levels as recited in claims 6-7 of the instant invention. It is noted that claims 6-7 recite 'and a patient having both high CRP and high Lp-PLA2 levels is indicative of heightened risk of CVD'. However, such recitation does not require steps to be performed and do not limit the claim scope (see MPEP section 2111.04). Packard specifically teach a multivariate assessment on the risk of a coronary event (Table 5). As such, the models used the variables including CRP and Lp-PLA2 (i.e. a combination of risk factors). Packard confirms that CRP and Lp-PLA2 are both indicators of risk of coronary heart disease (page 1152 'discussion' section 1st paragraph). Taken together, Packard teach the limitations of claim 1 including measuring levels of Lp-PLA2 and CRP (page 1149 'measurements' section 2nd paragraph), analyzing the risks (Table 5), and using the risks (page 1152 'discussion' section 1st paragraph, Table 5) thus meeting the limitations of claim 1 of the instant invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2,4-7,10-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Packard et al. (NEJM Oct 19 2000 v343 pages 1148-1155) and further in view of Rao et al. (US 2003/0120134).

As discussed above Packard teach that there are reports that C-reactive protein (CRP) levels are elevated in those at risk for coronary disease (page 1148 column 2 1st paragraph). Packard teach that lipoprotein-associated phospholipase A2 (Lp-PLA2, also known as platelet-activating factor acetylhydrolase) is a potential predictor of the risk of coronary heart disease (page 1148 column 2 2nd paragraph). Packard confirms that CRP and Lp-PLA2 are indicators of risk of coronary heart disease (page 1152 'discussion' section 1st paragraph). Thus the specific disease recited in claim 2 of the instant invention is met. Packard teach that the patient population includes patients with hypertension (table 1) thus meeting the limitation of the elected patient population. Packard teach that CRP and Lp-PLA2 were measured in aliquots of plasma collected from patients (page 1149 'measurements' section 2nd paragraph) thus the sampling (which is a step of the measuring process) was done simultaneously thus meeting the limitations of claim 4 of the instant invention. Packard also teach that separate enzyme-linked immunoassays were performed for CRP and Lp-PLA2 (page 1149 'measurements' section 2nd and 3rd paragraphs) thus the assaying (which is a step of the measuring process) was performed sequentially thus meeting the limitations of claim 5 of the instant invention. Packard teach that

Lp-PLA2 mass was measured (page 1149 'measurements' section 3rd paragraph) thus meeting the limitation of claim 11 of the instant invention. Packard teach that quintile ranges (i.e. divided into 5 classes) were established for the variables (page 1140 'statistical analysis' section 1st paragraph). Since there are 5 classes there are necessarily high and low levels as well as high, medium, and low levels as recited in claims 6-7 of the instant invention. It is noted that claims 6-7 recite 'and a patient having both high CRP and high Lp-PLA2 levels is indicative of heightened risk of CVD'. However, such recitation does not require steps to be performed and do not limit the claim scope (see MPEP section 2111.04). Packard specifically teach a multivariate assessment on the risk of a coronary event (Table 5). As such, the models used the variables including CRP and Lp-PLA2 (i.e. a combination of risk factors). Packard confirms that CRP and Lp-PLA2 are both indicators of risk of coronary heart disease (page 1152 'discussion' section 1st paragraph). Taken together, Packard teach the limitations of claim 1 including measuring levels of Lp-PLA2 and CRP (page 1149 'measurements' section 2nd paragraph), analyzing the risks (Table 5), and using the risks (page 1152 'discussion' section 1st paragraph, Table 5) thus meeting the limitations of claim 1 of the instant invention.

Packard does not expressly teach the use of ATP III guidelines as recited in claim 10.

Rao et al. teach systems and methods for screening for coronary heart disease (abstract). Rao teach that patients are assessed for risk for coronary heart disease based on factors (section 0032). Rao specifically teach that the Adult Treatment Panel (ATP III) has produced guidelines for risk. Rao teach the use of the guidelines in the system for screening for coronary heart disease.

Both Packard and Rao teach methods for assessing risk of coronary heart disease. Since there is evidence that cardiovascular risk and disease is under-treated (Rao section 0005) one would be motivated to use various methods and combinations of methods to assess risk of coronary heart disease. In particular one would be motivated to use the CRP and Lp-PLA2 risks and additionally use the ATP III guidelines as taught by Rao with the method of Packard thus meeting the limitations of the claims of the instant invention. It is noted that it is obvious to combine compositions each of which is taught by the prior art to be useful for the same purpose (see MPEP section 2144.06). Likewise is it obvious to combine risks (such as those associated with CRP, Lp-PLA2, and ATP III guidelines) for the purpose of assessing the risk of coronary heart disease.

It has been recently held that "Neither §103's enactment nor *Graham*'s analysis disturbed the Court's earlier instructions concerning the need for caution in granting a patent based on the combination of elements found in the prior art." KSR v. Teleflex, 550 U.S. ___, 82 USPQ2d 1385, 1389 (2007). The KSR court stated that "a combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." KSR at 1389.

Furthermore, The KSR court concluded that "obvious to try" may be an appropriate test under 103. The Supreme Court stated in *KSR*

> When there is motivation
>
> > "to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103." *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, ___, 82 USPQ2d 1385, 1397 (2007).

In the instant case all the claimed elements were known in the art as discussed above and one skilled in the art could have combined the elements by known methods and the combination would have yielded predictable results. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to RONALD T. NIEBAUER whose telephone number is (571)270-3059. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, alt. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ronald T Niebauer/
Examiner, Art Unit 1654

/Anish Gupta/

Primary Examiner, Art Unit 1654